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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/687,951	10/13/00	CLELAND J	M-9177-US

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EXAMINER	
KAM, C	
ART UNIT	**PAPER NUMBER**
1653	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/687,951	CLELAND ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 20-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17, 20-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *4* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 17 and 20-34 are pending.

Applicants' response filed on May 9, 2001 (Paper No. 7) has been fully considered. Claims 1-16 and 18-19 have been cancelled, claims 17 and 20 have been amended, and new claims 21-34 have been added.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1-20, under 35 U.S.C.112, second paragraph, is withdrawn in view of applicants' cancellation of the claims, amended claim 17 and making changes in the new claims.

Claim Rejections - 35 USC § 102(b) and 103(a)

3. The previous rejection of claims 1-6, 8-11, 13-14 and 17-20 under 35 U.S.C.102(b) as being anticipated by Igari *et al.*, is withdrawn in view of applicants' cancellation of the claim and applicants' response cited on pages 5 and 6 in Paper No:7.

4. The previous rejection of claims 1-13 and 15-19 under 35 U.S.C.102(b) as being anticipated by Machida *et al.*, is withdrawn in view of applicants' cancellation of the claim and applicants' response cited on pages 5 and 6 in Paper No:7.

5. The previous rejection of claims 1-20 under 35 U.S.C.103(a) as being unpatentable over by Igari *et al.* in view of Machida *et al.*, is withdrawn in view of applicants' cancellation of the claim and applicants' response cited on pages 5 and 6 in Paper No:7.

Claim Objections

6. Claim 29 is objected to because of the following informalities: "glucagons" is used in line 4 of the claim, it should be "glucagon". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 20 is rejected under 35 U.S.C. 112, first paragraph.

Claim 20 is rejected because the specification, while being enabling for a method for administering a biologically active agent comprising injecting the composition with particle size of 5-200 microns to a patient using a 23-gauge or smaller needle, does not reasonably provide enablement for a method for administering a biologically active agent comprising injecting the composition with particle size of < 1 mm using a 23-gauge or smaller needle. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 20 is drawn to a method for administering a biologically active agent comprising injecting the composition to a patient using a 23-gauge or smaller needle. The specification discloses microparticles used have a maximum dimension of < 1 mm (page 6, line 7), although the preferred microparticles have an average diameter of 5-200 microns (page 14, lines 4-5). The 23-gauge needle has an inside diameter of 0.318 mm (318 μm, see page T679 of Aldrich catalog (2000-2001)), which is suitable for injection of the microparticles with particle size of < 200 μm but not for all the particles having size of < 1 mm. Therefore, the claim needs to define

the microparticle size as to the bore size of needle. The skilled artisan would require additional guidance in order to make and use such microparticles in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the scope of the claims, the nature of the invention, and the amount of direction or guidance presented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 21-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the specification appears to define hyaluronic acid (see page 4, lines 21+) as part of or as a biologically active agent (see the definition proffered at page 6, lines 10+ of the current specification). Thus, claim 21 and claims dependent there to are indefinite as to whether or not hyaluronic acid was or was not part of an agent having in vivo activity, typically an activity that confers therapeutic, prophylactic, and/or diagnostic utility given the definition at page 4 of hyaluronic acid being found in the extracellular matrix of connective tissue. Thus, in claim 21, is item (a) included in item (b)(i) and/or (b) (ii)? For clarity, claim 28 should be cancelled in favor of inserting "polypeptide" in claim 21 in place of "agent". Claims 22-34 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

9. Claim 24 is indefinite because of the use of the term "a copolymer comprising biodegradable and non-biodegradable units". Note that Markush groups must be closed and "a copolymer comprising biodegradable and non-biodegradable units" is open language in regard to the amounts of each in the copolymer which are unrecited and make the copolymer undefined.

10. Claims 30 and 31 are indefinite because claim 30 recites the limitation "the polymeric matrix comprising the biologically active agent" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 21 cites particles comprising a biologically active agent, and a biocompatible polymeric matrix. The same rejection is also applied to claim 31.

11. Claim 32 is indefinite because of the use of the term "derivative". The term "derivative" renders the claim indefinite, it is unclear what kind of ester derivative, amide derivative, lactide derivative, acyl derivative, polyethylene glycol derivative or water-insoluble derivative of hyaluronic acid is intended as compared to hyaluronic acid.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 17, 20-28, 30-31 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Machida *et al*. (EP 0,263,490) in view of syringe section (page T679) of Aldrich catalog (2000-2001).

Machida *et al*. teach a sustained-release particulate preparation is obtained by mixing a biodegradable polymer in an organic solvent with a biologically active agent to form a solution, suspension or emulsion, and the mixture is then mixed with an aqueous solution comprising a natural high molecular weight of sugar such as hyaluronic acid to prepare fine particles containing the biologically active agent (column 4, lines 17-30; and Example 1 and 3). The particulate preparation has a particle size of 150 μm or less (column 2, line 8-13), which can be reconstituted with saline solution and is suitable for injection. However, Machida *et al*. fail to disclose the type of syringe needle used for injection. The Aldrich catalog shows a 23-gauge syringe needle has an inside diameter of 0.318 mm (318 μm), which is suitable for injection of the particulate preparation with particle size of 150 μm or less. At the time of invention was made, it would have been obvious to one of ordinary skill in the art to use the particulate preparation taught by Machida *et al*. with a syringe of 23-gauge needle to administer a biologically active agent because one of ordinary skill in the art would have been motivated to check whether the particulate preparation containing the biologically active agent can be delivered with a smaller needle in order to improve the injectability of particulate preparation, which meet the criteria of claims 17, 20-28, 30-31 and 34. Thus, the combined references result in the claimed invention and was, as a whole, prime facie obvious at the time the claimed invention was made.

In response, applicants argue that Machida *et al*. teach a method of making particles, but no particles containing a biological polymer and a biologically active agent are described (page 6, second paragraph of Paper No. 7), and hyaluronic acid is used as a medium for precipitating the particles containing the active agent, as well as the particles produced by this method are

administered by injecting a mixture of the particles with physiological saline (page 5, paragraph 5 of Paper No. 7). However, the argument is not persuasive because Machida *et al*. have described the particulate preparation of the mixture of biodegradable polymer in an organic solvent with a biologically active agent (see Examples 1 and 3), although the particulate form of the mixture is not particularly mentioned in the Example, the solution, suspension or emulsion form has been indicated when a biodegradable polymer in an organic solvent is mixed with a biologically active agent (column 4, lines 22-23 and 27). The suspension or emulsion of the mixture is the indication of the formation of particles. When the mixed solution is added to aqueous solution of hyaluronic acid, the microspheres containing the active agent are formed, collected by centrifugation, and lyophilized as powder (see Example 1). Since the particulate preparation is obtained as a powder, it is reconstituted with saline solution for injection (see Test Example 1, column 10), the resulting particulate preparation which has a particle size of 150 μm or less is suitable for injection with a 23-gauge syringe needle, thus meets the criteria of the claimed invention.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers

for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D.
Patent Examiner

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July 4, 2001

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